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Rapid Communication

A convenient synthesis of 5,11-dihydro-5,11- dimethyl-6-trifluoromethylindolo[3,2-*b*]carbazole

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On treatment with TFAA, both *N,N'*-dimethyl-3,3'-diindolylmethane and *N*-methylindole-3-methanol give 5,11-dihydro-5,11-dimethyl-6-trifluoromethylindolo[3,2–*b*]carbazole along with three other products.

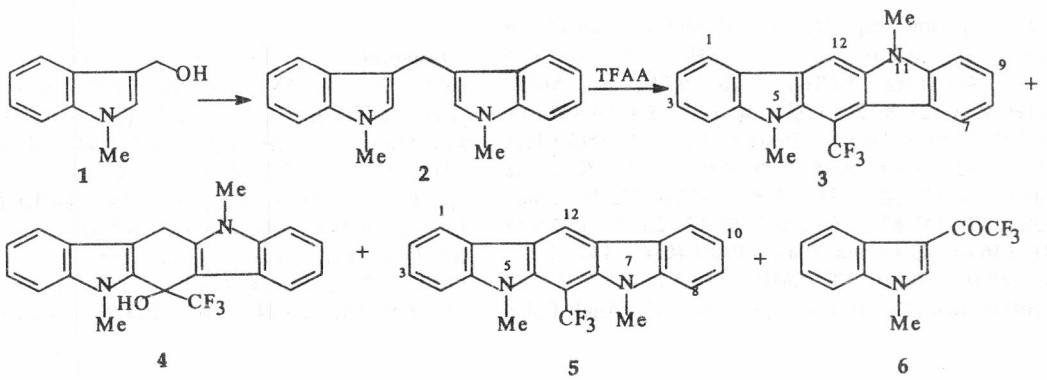
Trifluoromethylated organic compounds have been the subject of much attention in recent years owing to their unique physical and biological properties.[1] As some of the indolocarbazoles show biological activities,[2] it was our interest to synthesise such compounds having a trifluoromethyl group at different positions. In this endeavour, we first chose the reaction of 3,3'-diindolylmethanes (readily available from 3-indolylmethanols)[3] with trifluoroacetic anhydride (TFAA), as the former can supply two nucleophilic indole moieties and the latter an electrophilic carbonyl carbon and a trifluoromethyl group. A preliminary account of the interesting aspects of this study is presented herein.

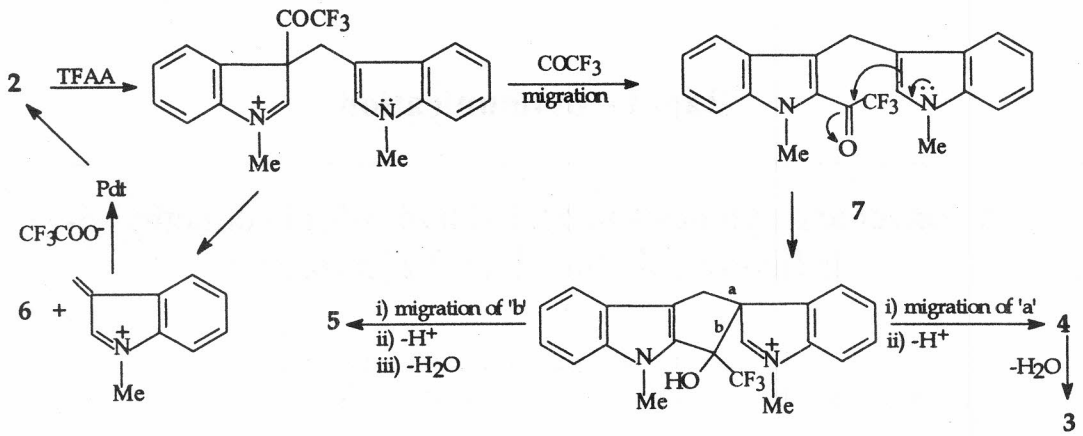
N,N'-Dimethyl-3,3'-diindolylmethane **2** on treatment with TFAA (Et_2O, room temperature) underwent complete conversion within 16 hr, yielding four products, which after chromatographic separation (silica gel) followed by characterisation[4] were found to be 5,11-dihydro- 5,11 -dimethyl- 6-trifluoromethylindolo[3,2-*b*]carbazole **3** (22 %), 5,6,11,12-tetrahydro-5,11-dimethyl-6-hydroxy-6-trifluoromethylindolo[3,2-*b*]carbazole **4** (10%), 5,7-dihydro-5,7-dimethyl-6-trifluoromethylindolo[2,3-*b*]-carbazole **5** (1%) and *N*-methyl-3-trifluoroacetylindole **6** (32%). The compound **4** underwent quantitative transformation to **3** with ethanolic HCl (room temperature, 10 min.).

As **2** was prepared by heating *N*-methylindole-3-methanol **1** in aqueous methanol,[3b] we envisaged that this conversion step could be carried out *in situ* and our objective might be fulfilled by replacing **2** by **1**. Thus, we treated **1** with TFAA at room temperature and obtained the same products as in the previous case [**3**, 13%; **4**, 9%; **5**, 1%; **6**, 2%]. Taking the easy and quantitative transformation of **4** to **3** into account, it may be concluded that the overall yield of **3** in both the reactions is satisfactory. The simplicity of the conditions of the reactions makes them attractive

Considering the findings of Jackson *et al.*[5] on acylation and related reactions of 3-alkylindoles, the mechanistic path delineated in **Scheme I** may be suggested for the formation of **3-6**. However, the possibility of formation of **7** by direct acylation at 2-position of **2**[6] cannot be ruled out.

Finally, it may be mentioned that we have developed an expedient synthesis of the indolocarbazole **3**. There is a scope of the synthesis of a number of analogues of **3** by variation of the indole moiety and the *N*-alkyl group.





Scheme I

Acknowledgement

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4 **3**: Yellow prisms, mp 212 °C; IR and UV spectra as expected; ^{1}H NMR ($CDCl_3$): δ 3.9(3H, s, 11-CH_3), 3.94 (3H, q, *J*=3.16Hz, 5-CH_3), 7.25-7.6(6H, m, Ar-H), 8.10(1H, s, H-12), 8.12-8.15(1H, m, H-1), 8.4-8.43(1H, m, H-7); ^{13}C NMR ($CDCl_3$): δ29.05(11-CH_3), 35.75(5-CH_3), 102.52 (C-12), 108.13 (C-4), 109.64 (C-10), 118.63 (C-2), 119.43 (C-1), 119.60 (C-8), 120.86 (C-12a), 122.49 (C-6a), 124.29 (C-7), 125.62 (C-6b and 12b), 126.26 (C-3), 126.81 (C-9), 136.48 (C-4a and 10a), 136.59 (C-6), 142.11 (C-11a), 145.09 (C-5a); ^{19}F NMR ($CDCl_3$): δ –51.27 (q, *J*=3.10Hz). MS (CI): m/z 352 (31.3 %, M^+). Anal. Calcd for $C_{21}H_{15}F_3N_2$ (352.36): C, 71.58; H, 4.29; N, 7.95. Found: C, 71.48; H, 4.37; N, 7.71 %. **4**: mp 230 °C (d). **5**: mp 210 °C. **6**: mp 103 °C [reported[7] mp 104 °C], gave satisfactory analytical and spectral data. In the ^{1}H NMR spectrum of **3**, only one N-Me experienced a six-bond H-F coupling but in the ^{1}H NMR of **5** both the N-Me's resonating at δ 3.99 (6H, q, *J*=2.68Hz) experienced such coupling.[7]

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SUPPLEMENTARY DATA

Compound 3 — IR(KBr): 1610, 1500, 1480, 1415, 1355, 1315, 1285, 1215, 1195, 1170, 1150, 1110, 1060, 1045, 900, 800, 740 cm^{-1}; UV(ether): 239.5 (log ε 4.02), 260 (4.02), 283 (4.21), 334.5 (4.0), 349 (4.18), 396.5 (3.33), 418.5 nm (3.84); MS (CI): m/z 353 (100 %), 352 (31.3, M^+), 333 (10.8, M–F), 170 (7.7), 42 (17).

Compound 4 — IR(KBr): 3500 (OH), 1610, 1470, 1170, 1085, 970, 740 cm^{-1}; UV(ether): 239 (log ε 4.10), 279 nm (4.18); ^{1}H NMR ($CDCl_3$): δ 2.80 (1H, s, 6-OH, exchangeable with D_2O), 3.68 (3H, s, 11-CH_3), 3.94 (2H, s, 12-CH_2), 4.0 (3H, s, 5-CH_3), 7.2-7.42 (6H, m, Ar-H),7.63-7.65 (1H, m, H-1), 7.89-7.91 (1H, m, H-7); ^{13}C NMR ($CDCl_3$): δ 20.43 (C-12), 29.38 (11-CH_3), 31.92 (5-CH_3), 106.98 (C-6), 109.08 (C-4), 109.77 (C-10), 110.34 (C-12a), 118.52(C-1), 119.55 (C-7), 120.16 (C-3), 120.30 (C-9), 121.50 (C-2), 122.97 (C-8), 125.16 (C-6a), 126.24 (C-12b), 128.98 (C-6b), 130.52 (C-11a),

137.61 (C-4a), 137.81 (C-10a), 139.02 (C-5a); MS (FAB): m/z 371 (41 %), 370 (59, M^+), 369 (20), 353 (17, M–OH), 302 (24.69, M–CF_3H), 301 (100, M–CF_3), 299 (11), 285 (9), 284 (13), 240 (35). Anal. Calcd for $C_{21}H_{17}F_3N_2O$ (370.37): C, 68.10; H, 4.62; N, 7.56. Found: C, 68.23; H, 4.49; N, 7.42 %. ^{19}F NMR ($CDCl_3$): δ –76.56 (s).

Compound 5 — IR(KBr): 1625, 1600, 1490, 1470, 1445, 1375, 1310, 1255, 1200, 1170, 1090, 1065, 973, 750 cm^{-1}; UV(ether): 244 (log ε 4.65), 274 (4.35), 299 (4.77), 304 (4.23), 374.5 nm (4.28); ^1H NMR ($CDCl_3$): δ 3.99 (6H, q, *J*=2.68 Hz, 5 and 7-CH_3), 7.30-7.53 (6H, m, Ar-H), 8.15-8.17 (2H, m, H-1 and H-11), 8.83 (1H, s, H-12); MS (CI): m/z 354 (22.7 %), 353 (100), 352 (40, M^+), 333 (8, M–F), 170 (13), 61 (7), 42 (13). Anal. Calcd for $C_{21}H_{15}F_3N_2$ (352.36): C, 71.58; H, 4.29; N, 7.95. Found: C, 71.71; H, 4.19; N, 7.81 %.